

**REMARKS**

Reconsideration is requested.

Claims 7, 11-13, 19 and 22-36 have been canceled, without prejudice.

Claims 37-50 have been added. No new matter has been added. Support for the amended claims may be found throughout the specification.

Claims 1-6, 8-10, 14-18, 20-21 and 37-50 are pending.

Attached is/are PTO-1449 Form(s) listing references included in the Examiner's search notes obtained by the undersigned from the Image File Wrapper (IFW) of the USPTO PAIR page associated with the above-identified application. The Examiner is requested to return an initialed copy of the attached PTO-1449 Forms, pursuant to MPEP § 609, to confirm that the Examiner has considered the references of the Examiner's search which are now contained in the public record.

The attached PTO-1449 Forms do not include a listing of the sequence comparisons contained in the following:

thirteen (13) page "US-10-018-604-2.rag" search;  
sixteen (16) page "SU-10-018-604-1.rng" search;  
eleven (11) page "US-10-018-604-1.rni" search;  
twelve (12) page "US-10-018-604-1.rnpb" search  
nine (9) page "US-10-018-604-2.rai" search;  
seven (7) page "US-10-018-604-2.rapb" search;  
eight (8) page "US-10-018-604-2.rpr" search;  
eleven (11) page "US-10-018-604-2.rsp" search;

nine (9) page "US-10-018-604-2.rspt" search;  
eight (8) page "US-10-018-604-1.rag" search;  
six (6) page "US-10-018-604-4.rai" search;  
five (5) page "US-10-018-604-4.rapb" search;  
four (4) page "US-10-018-604-4.rpr" search;  
nine (9) page "US-10-018-604-4.rsp" search; and  
six (6) page "US-10-018-604-4.rspt" search,

which were also retrieved from the IFW, as the undersigned is uncertain of the basis of these searches and/or how to list the information considered by the Examiner in PTO-1449 Forms.

The Examiner is requested to provide PTO-892 Forms which detail the information considered by the Examiner, especially with regard to the search results included in the electronic records of the Patent Office.

Of particular interest from the Examiner's search are U.S. Patent Nos. 5,296,376 and 6,271,033, copies of which are attached. U.S. Patent No. 6,271,033 is a continuation of U.S. Patent No. 5,296,376. A copy of the Transaction History of the file histories of each of these patents and their parent application is also attached.

The claims of U.S. Patent No. 6,271,033 issued August 7, 2001. U.S. Patent No. 6,271,033 issued from application Serial No. 08/162,288, filed December 7, 1993, which is a continuation of application Serial No. 07/621,714, filed on December 5, 1990 (which issued as U.S. Patent No. 5,296,376 on March 22, 1994), which is a continuation-in-part of application Serial No. 07/119,614, filed November 12, 1987, which is a continuation

of application No. PCT/GB90/01827, filed November 26, 1990, and claims benefit of GB 86262879, filed November 11, 1986 and GB 8927048, filed November 30, 1989.

EP 0271,988, which is already of record, also claims benefit of GB 8626879.

The disclosure of U.S. Patent No. 6,271,033 was publicly available at least as early as March 22, 1994, in the form of U.S. Patent No. 5,296,376.

The present application is a 371 U.S. national phase of PCT/IB00/00869 filed June 15, 2000, which claims benefit of UK 9914209.3, filed June 17, 1999. The disclosure of U.S. Patent No. 6,271,033, in at least the form of U.S. Patent No. 5,296,376, was available to the public at the filing date of the priority application of the present application.

The claims of U.S. Patent No. 6,271,033, granted by the U.S. Patent Office, and hence determined to have been described and enabled by the disclosure of U.S. Patent No. 6,271,033, provide a method for modifying the production of a target gene product in a plant cell wherein the method comprises transforming the plant cell with a construct comprising a recombinant DNA sequence coding for only part of the target gene product wherein the target gene product is a fruit ripening enzyme. The claims of U.S. Patent No. 6,271,033 further provide the above-described process wherein the target gene product is any of PG, pectin esterase, galactosidase, glucanase, xylanase or cellulase.

The applicants submit that the attached U.S. No. 6,271,033 is evidence, if not conclusive evidence, that methods of silencing PG in a host cell were well known to those of ordinary skill in the art at the time of the present priority application was filed. The attached U.S. Patent No. 6,271,033 is also acknowledgement by the Patent Office that specific host cells or sequences were not required to practice the claimed method.

The Examiner will appreciate, for example, from the attached Transaction Histories, that application Serial No. 07/119,614, i.e., the grandparent of the application which issued as U.S. Patent No. 6,271,033, was involved in a two (2) year interference proceeding before the Board of Appeals and that the claims of U.S. Patent No. 6,271,033 were, apparently, also considered by the Board of Appeals. The attached Transaction Histories are submitted to demonstrate that the subject matter of U.S. Patent Nos. 6,271,033 and 5,296,376, were extensively considered by the Patent Office Examiners and Board of Appeals.

The presently claimed invention provides, as described at page 7 of the specification, for example, high molecular weight de-esterified pectin. The present applicants have appreciated that, in a naturally-occurring process of pectin degradation, demethylated pectins (i.e., pectins which have been "treated" with PME) are a substrate for PG, which substantially reduces the length of the pectin backbone, and hence the molecular weight of the pectins. The present applicants have discovered that pectins produced from treatment with a PME activity in an environment of reduced PG activity have a number of novel properties. Specifically, as demonstrated in the examples of the present application, the storage properties (i.e., sedimentation, particle size, separation, viscosity, etc.) of products containing modified pectins produced according to the presently claimed were superior to products which contained commercially available, pectins which were not modified according to the present invention.

The Section 112, first paragraph "written description" and "enablement", rejections stated on pages 3-7 of the Office Action dated August 31, 2004, are

traversed. Reconsideration and withdrawal of the rejections are requested in view of the above, the attached, and the following further comments.

The Examiner indicates that the specification only describes, based on "a single representative species" a method of modifying pectin by

"(i) providing a tomato plant host having native pectin methyl esterase (PME) and polygalacturonase (PG) activity; (ii) transforming said host by silencing PG activity, wherein the PG activity is silenced by expression of a nucleic acid sequence of SEQ ID Nos. 1 or 4 in an antisense orientation, thereby providing increased PME to PG ratio; (iii) isolating or preparing a PME extract from the transformed plant; (iv) treating the pectin with PME extract, and (v) isolating the de-esterified pectin." See, page 4 of the Office Action dated August 31, 2004.

As noted above however, the applicants submit that methods of silencing PG activity, as well as other fruit ripening related enzymes, in tomato and other plant cells, without the use of expression of SEQ ID NOS: 1 or 4 of the present application in an antisense orientation, were available and known to those of ordinary skill in the art, and acknowledged by the Patent Office, at the time the present priority application was filed. See, claims of attached U.S. Patent No. 6,271,033.

The present applicants should not be required to teach and/or describe methods used in the presently claimed invention which were known to those of ordinary skill in the art prior to the filing date of the present priority application. No "additional representative species" should be required of the present applicants, as suggested by the Examiner, to adequately describe those aspects of the presently claimed invention which was previously known.

Similarly, the applicants submit that the present specification, when taken with the generally advanced level of skill in the art, teaches one of ordinary skill how to make and use the presently claimed invention.

The Examiner's reference to and reliance on "Grierson et al (1986, Nucleic Acid Reviews, 14, p 8595-2603, IDS)" (see, page 6 of the Office Action dated August 31, 2004) is not understood and clarification is requested in the event the Examiner continues to rely on the same to reject the claims. Initially, the applicants note that there is no "Grierson et al (1986)" reference of record in the undersigned's file. The Examiner is requested to forward to the undersigned a copy of any IDS in the Examiner's file which lists a Grierson et al reference, along with a copy of the reference. The applicants note that the cited Grierson et al reference was apparently published thirteen (13) years prior to the filing of the present priority application (i.e., 1986 compared to 1999), such that Grierson et al may not be the best indication of the level of skill in the art at the time of the priority document filing.

More importantly, the Examiner is understood to be relying on Grierson et al for an alleged teaching that use of an antisense sequence corresponding to "a natural plant gene has been found to be more effective and widely used to control plant biochemistry or development". See, page 6 of the Office Action dated August 31, 2004. The more recent teaching of a Donald Grierson, i.e., the attached U.S. Patent No. 6,271,033, states the following:

"We believe that the mechanism of inhibition is independent of the nature of the gene or gene product. Thus in principle any the production of any kind of gene product may be inhibited." See, column 2, lines 43-46 of U.S. Patent No. 6,271,033.

The additional disclosure of PG sequences, or any pectinesterase, galactosidase, glucanase, xylanase or cellulase, partial or complete sequences in U.S. Patent No. 6,271,033 were not considered by the Patent Office to be required to make or use the method claimed in U.S. Patent No. 6,271,033. More should not be required of the present applicants. The presently claimed invention is supported by an enabling disclosure.

Withdrawal of the Section 112, first paragraph, rejections of claims 1-23 is requested.

The Section 112, second paragraph, rejection of claims 1-14 stated on page 7 of the Office Action dated August 31, 2004, is obviated by the above amendments.

The Section 112, second paragraph, rejection of claims 1-23 stated in paragraph 10 on page 8 of the Office Action dated August 31, 2004, is traversed. One of ordinary skill in the art will appreciate that modified pectin may be made according to the claims without requiring isolation of the pectin from the PME extract. The PME activity may be neutralized, for example, by heating and the modified pectin utilized without requiring "isolating" of the modified pectin. The claims are definite and complete without further amendment.

The Section 112, second paragraph, rejection of claim 2 stated in paragraph 11 of page 8 of the Office Action dated August 31, 2004, is obviated by the above amendment. Withdrawal of the rejection is requested.

The Section 103 rejection of claims 1-23 over "EP 0532060 A1 A2 [Bridges et al, 1993 IDS]" and WO 97/03574 [Christensen et al, Feb. 6, 1997, IDS] is traversed.

Reconsideration and withdrawal of the rejection are requested in view of the above, attached and the following distinguishing comments.

Initially, the undersigned has not located an IDS (PTO-1449 or PTO-892) listing "EP 0532060 A1 A2" cited by the Examiner. A review by the undersigned of the USPTO IFW available through PAIR does not reveal a PTO-1449 or PTO-892 Form listing "EP 0532060 A1 A2" or a copy of the reference. The Examiner is requested to provide the undersigned with a copy of the noted IDS and cited reference and to have the same added to the IFW if not already contained therein.

The applicants note that the Examiner's PTO-892 refers to an alignment between applicants SEQ ID NO:1 and Accession No. A15981 and a second alignment between applicants SEQ ID NO:2 and Accession No. AAR32107 which are believed to refer to "Result 3" of the above-noted "US-10-018-604-1.rge" (Accession No. A15981) which the search indicates was disclosed in EP 0271988-A1, 22-Jun-1988 of Bridges et al (see, page 4, left column of "US-10-018-604-1.rge"); and "Result 3" of the above-noted "US-10-018-604-2.rag" (Accession No. AAR32107) which the search indicates was disclosed in EP 0532060-A1 of Bridges et al (1993). The Examiner is again requested to provide a complete record of any art and/or information considered by the Examiner by listing the same on PTO-892 Forms and returning an initialed copy of the attached PTO-1449 Form, pursuant to MPEP § 609.



Bridges et al apparently teaches that the sequences of the present disclosure were known and that antisense technology may be used to delay softening of tomato fruit.<sup>1</sup>

As admitted by the present Examiner, Bridges et al (i.e., EP 0532060) do not teach de-esterification of pectin or modifying pectin. See, page 10 of the Office Action dated August 31, 2004. Presumably Bridges et al further fail to teach the advantages of de-esterified pectin, as discovered by the present applicants. Specifically, Bridges et al will also likely fail to teach the advantages of the use of a PME extract which has been prepared in an environment of decreased PG activity for de-esterification of pectin, as discovered by the present applicants and disclosed in the above-identified application.

Christensen fails to cure these apparent deficiencies of the cited Bridges et al document.

Christensen is described by the Examiner to teach enzymatic de-esterification of pectin using recombinant pectin methyl esterase from orange. The Examiner admits that Christensen fails to teach "the transformation of a host plant having the native enzyme activities of PG & PME, wherein the PG expression is blocked or silenced using antisense or complimentary molecule of SEQ ID NO:1 or 4." See, page 10 of the Office Action dated August 31, 2004.

Not only does Christensen fail to teach such a transformation, neither Christensen nor Bridges et al (apparently) would have motivated one of ordinary skill in the art to make the presently claimed invention. The Examiner's apparent collection of

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<sup>1</sup> There is nothing in the current record to support the Examiner's interpretation as the sequence alignment of the IFW available through PAIR only provides a sequence. In the event the Examiner

parts of the claimed invention (i.e., "the combined teachings of the prior art cited above teach all the elements of the claimed invention." id.) should not be sufficient to establish a *prima facie* case of obviousness. The cited art fails to provide motivation to have made the claimed invention or to predict the unobvious advantages of doing so. The claimed invention is submitted to be patentable over the combination of cited art and withdrawal of the Section 103 rejection is requested.

A Notice of Allowance and PTO-892 Forms listing all of the information considered by the Examiner, along with return of an initialed copy of the attached PTO-1449 Forms, are requested. The Examiner is requested to contact the undersigned in the event anything further is required.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

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continues to rely on EP 0532060 to reject the claims, the Examiner is requested to provide a copy of the reference, and make the reference of record along with a further non-final Office Action